Protein Complexes and Functional Modules in Molecular Networks

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Proteins, nucleic acids, and small molecules form a dense network of molecular interactions in a cell. Molecules are nodes of this network and the interactions between them are edges. The architecture of molecular networks can reveal important principles of cellular organization and function, similarly to the way that protein structure tells us about the function and organization of a protein. Computational analysis of molecular networks has been primarily concerned with node degree or degree correlation, and hence focused on *single/two-body* properties of these networks. Here, by analyzing the *multi-body* structure of the network, we discovered molecular modules that are densely connected within themselves but sparsely connected with the rest of the network. Comparison with experimental data and functional annotation of genes showed that such modules correspond either to protein complexes (splicing machinery, transcription factors, etc.) or to dynamic functional units (signaling cascades, cell-cycle regulation, etc.). These modules are highly statistically significant, as is evident from comparison with random graphs, and are robust to noise in the data. Our results provide strong support for the network modularity principle introduced by Hartwell et al, suggesting that the found modules constitute the "building blocks" of molecular networks.